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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,246	01/03/2002	Toshiaki Takezawa	2001-1784A	1296

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 03/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,246	TAKEZAWA ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8,9 and 11-25* is/are pending in the application.

4a) Of the above claim(s) *14-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,3-6,8,9,11-13,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-6, 8, 9 and 11-13 as amended and new claims 24 and 25 (12/08/2005) are pending and under examination.

Claims 14-23 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected invention(s).

Claim Rejections - 35 USC § 112

Claims 1, 3-6, 8, 9 and 11-13 as amended new claims 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 as amended is rendered indefinite by the phrase "further" (line 4) because the use of this language in the context of first independent claim is improper and it fails to limit the claimed invention. This language encompasses at least two compositions such as a composition without a culture and a composition with a culture. Thus, it is uncertain what are components of the claimed composition as intended.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, 8, 9, 11-13 as amended and new claim 25 remain/are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,919,624 (Ried et al.) as explained in the prior office action and for the reasons below.

Claims are directed to a composition wherein the composition comprises 1) an animal tissue section with thickness from 0.5 to 50 μm that is attached to a support and 2) a culture medium. Some claims are further drawn to the use of various support materials including glass, plastic, etc. Some claims are further drawn to the use of tissue that is fixed, processed for acellularization, embedded. Some claims are directed to the use of tissue derived from mammalians.

US 5,919,624 discloses a composition comprising 1) cervical tissue sections having thickness 4 μm or 8 μm or 50 μm depending on the intended tissue testing and attached to various support materials including glass or plastic containers (col. 12, lines 5-25) and 2) paraffin for embedding animal tissues that would be "a culture medium" within the broadest reasonable meaning of the term "culture medium". The claimed culture medium is generic and it is not limited to any specific components. The tissue sections are fixed, paraffin-embedded and, thus, they are processed for acellularization within the meaning of the claims. The tissue sections are derived from patients or mammalian animals. The limitations drawn to the use of tissues derived from either born or unborn mammals do not provide for any structural and functional differences from the cited tissues that collected from adult patients because the claimed tissue is generic and the age or maturity related differences, if any, cannot be determined. With respect to the new limitation drawn to a step of rinsing with a culture medium, it is noted that final characteristics of "rinsed" tissue section are not claimed. The cited tissues were stained and embedded and, therefore, rinsed. With respect to the new limitation "the tissues section does not require further treatment for the growth or culture of animal cells thereon", it is noted that this limitation does not bear any structural elements and considered to be an intended use limitation. A recitation of

the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.

Thus, the cited patent is still considered to anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-6, 8, 9 and 11-13 as amended and new claims 24 and 25 remain/are rejected under 35 U.S.C. 103(a) as being obvious over WO 99/12555 (Badylak et al.) and Mori et al. (Anat. Embryol. (1999) 199:319-327) taken with US 5,919,624 (Ried et al.) and US 3,785,234 (Sitte) as explained in the prior office action and for the reasons below.

Claims are directed to a composition for seeding and culturing animals cells wherein the composition comprises two major components 1) an animal tissue section with thickness from 0.5 to 50 μm that is attached to a support and 2) a culture medium. Some claims are further drawn to the use of various support materials including glass, plastic, etc. Some claims are further drawn to the use of tissue that is fixed, treated with reagents or embedded. Some claims are directed to the use of tissue derived from fetal or postnatal mammalian animals. Some claims are further drawn to incorporation of third component into the composition such as live animal cells.

The reference by Mori et al discloses a tissue section-containing carrier or a tube wherein the tube comprises an animal tissue section that is a preparation of mouse fetal or postnatal liver tissue section. The liver tissue is cut into 240 μm thick slices. The tissue sections are mounted in a plasma clot on cover glass and, thus, attached to the support treated in order to promote tissue adhesion (page 320, col. 1, par. 2) and/or embedded in resin. The liver tissue sections are live and growing. The liver tissue sections are further fixed with methanol and treated with antibody (page 320, col. 2, par. 3).

WO 99/12555 discloses a cell culture carrier or a well plate that is used for animal cell culture and that comprises an animal tissue section such as submucosal tissue attached to a plastic support or holder and a complete culture medium (example 3, pages 17-18). The tissue section of the cited patent has been demonstrated to support grown of other cells (page 18, at results). The plastic holder is flat in order to keep the tissue flat and thus, it is treated to promote tissue adhesion within the meaning of instant claims. The submucosal tissue is treated with enzyme galastosidase to remove surface epitopes and, thus, to modify tissue microstructure within the meaning of the instant claims. The cited patent teaches that the collection of submucosal tissue preparations includes freezing (page 12, line 29) and also includes treatment with antibodies (page 14, line 4) at least for the purpose of quality control of the submucosal tissue samples. The submucosal tissue preparations are obtained from mammalian animals (page 4, line 18) and might be 100-200 micrometers (page 4, lines 30-31). Although the cited document does not explicitly indicate whether born or unborn animals were used for tissue collections, it is reasonably to assume that both born and unborn animals have submucosal tissues and, thus, the submucosal tissue preparations used in the cell culture carrier of cited

patent meets the meaning of instant claims 12 and/or 13. The submucosal tissue preparations are rinsed with salt solution and treated with a complete cell culture medium (page 18, lines 2-5).

Therefore, the reference by Mori et al discloses that tissue is cut into 240 μm thick slices. WO patent is not particularly clear about thickness of final tissue section that is used as support for culturing cells. However, both preparations are capable to maintain animal cell culture growth regardless their thickness.

The additional references demonstrate that equipment to cut thin tissue sections is available (US 3,785,24 at col.1, lines 10-15) and that thickness of tissue sections is modified accordingly to the intended testing (see US 5,919,624 at col. 12, lines 5-20).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to obtain tissue sections of various thickness with a reasonable expectation of success in culturing animal cells. One of skill in the art would have been motivated to modify thickness of tissue sections with regard to design of culture containers, for example, or with regard to further evaluation of tissue sections as suggested by US 5,919,624 for various testing protocols. One of skill in the art would have been motivated to decrease thickness of tissue sections for the expected benefits in visual evaluation of tissue section under microscope, for example.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicants' arguments filed 12/08/2005 have been fully considered but they are found not persuasive.

With regard to the claim rejection under 35 U.S.C. 102(b) as being anticipated by US 5,919,624 (Ried et al.) applicants argue that the cited paten does not teach tissues section in contact with a culture medium (response page 8). However, the claimed culture medium is generic and it is not limited to any specific components. The cited composition comprises paraffin for embedding animal tissues that would be "a culture medium" within the broadest reasonable meaning of the term "culture medium". Moreover, paraffin is a carbon source for culturing living cells, for example, for culturing microbial cells.

With regard to the claim rejection under 35 USC § 103 applicants' main argument is directed to the idea that the combined teaching of the cited references would not motivate ordinary skill in the art to prepare a tissue section accordingly to the claimed invention including the use of thickness 0.5-50 μm (response page 9). This argument is not found persuasive because prior art demonstrates culturing cells on tissue sections with various thicknesses and because methods of cutting tissues into sections of various thicknesses including 0.5-50 μm are known in the prior art. One of skill in the art would have been motivated to optimize or to modify the thickness of tissue sections with regard to a particular design of a culture container; or with regard to a particular animal tissue that is used for making a tissue section; or as intended for further evaluation of tissue sections as suggested by US 5,919,624 for various testing protocols, for example. One of skill in the art would have been motivated to decrease thickness of tissue

sections for the expected benefits in visual evaluation of tissue section under microscope, for example.

The criticality of tissue section being 0.5-50 μm thick is uncertain as argued and as disclosed by applicants. The presently claimed "tissue section" is a generic tissue section and it is not limited to any specific tissue or any animal organ. Moreover, in the light of as-filed specification the claimed thickness slices 0.5-50 μm appears to be a thickness of a resin-embedded and frozen tissue section as disclosed (page 24, for example). The final thickness of thawed tissue sections that would be combined with animal cells as intended for seeding and culturing animal cells is unknown as disclosed. However, thawing, rinsing and incorporation of a culture medium would obviously result in some swelling of tissues to at least some degree. Thus, the thickness would be modified and/or increased. Therefore, there would not be any critical structural differences that appear to be argued. Applicants' arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

February 27, 2006

VERA AFREMOVA

PRIMARY EXAMINER